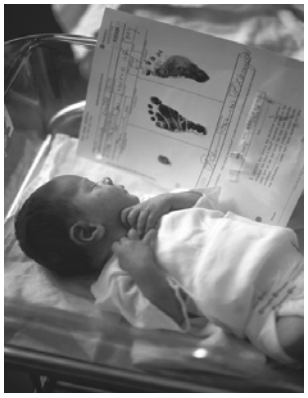

NEBRASKA NEWBORN SCREENING PROGRAM UPDATE

This update is being sent to health care practitioners responsible for ensuring the collection of the newborn dried blood spot filter paper specimen, or who may follow infants and children with these disorders. Blood-spot screening includes disorders in several classes: metabolic, endocrine, hemoglobin and cystic fibrosis.

Nebraska's Required Blood-Spot Panel Changes in January 2006

Beginning with specimens received at the newborn screening laboratory (Pediatrix) on January 2nd 2006, all newborns will be screened for **8 required** disorders. **Cystic Fibrosis and Congenital Adrenal Hyperplasia** will be added. Therefore, beginning with late December births whose specimens will be received at the laboratory in January, physicians should be informing parents about the required and supplemental screen. The cost of the screening will increase from $30.75 to $35.75 (laboratory testing and fees -this does not include hospital charges). The required screen will now include:

Biotinidase Deficiency
Congenital Primary Hypothyroidism(CPH)
Congenital Adrenal Hyperplasia (CAH)
Cystic Fibrosis (CF)
Galactosemia
Hemoglobinopathies (e.g. Sickle Cell)
MCAD
PKU

Testing for the supplemental disorders detected by tandem mass spectrometry will continue to be available at no additional charge, and with no additional blood needed. Parents will still need to provide their consent to receive these test results.

Birthing hospitals will receive the revised "Parent's Guide to Your Baby's Newborn Screening" in December to assist physicians with patient education.

Ideally patient education about newborn screening should occur during the third trimester of the pregnancy. If you would like to receive free supplies of the "Parent's Guide" at your clinic, please contact the newborn screening program at 402 471-9731 or newborn.screening@hhss.ne.gov.

In this issue…

Communicating Results to Parents/What to do with Positive Reports

Screening tests are designed to separate those newborns who are at higher risk of having one of the conditions screened from those who are not, so that follow-up activities can be undertaken for definitive diagnosis and early treatment. Screening algorithms are designed to minimize the number of false positives while reducing the risk of missing an affected newborn.

Screening technologies have evolved over the years for improved sensitivity and specificity. One tool to accomplish this is called second-tier testing or additional testing done at the lab on the initial specimen. While these tests provide the added value of improved specificity and sensitivity, using them as second tier rather than primary screens helps newborn screening remain one of the most cost effective and beneficial prevention programs.

The laboratory screening algorithms for both CF and CAH include second-tier testing for a subset of infants on the initial screen. Second-tier tests for CF include DNA testing on initial specimens that have elevated immuno-reactive trypsinogen (IRT) levels, or for newborns at risk of being missed because IRT's may be falsely low in infants with meconium ileus. Second-tier tests for CAH include an organic extraction 17-alpha hydroxy projesterone (17-OHP). This is done to reduce the high false positive rate common in specimens from premature babies due to interferences in the 17-OHP.

With these improvements we can customize recommended responses to screening results based on risk. Understanding relative risk, will help the physician communicate the information to the parents. For example in many cases the Nebraska Newborn Screening Program (NNSP) will recommend repeat testing of a new filter paper specimen because the screening results suggest a possible but not probable condition. In other words, it will be important to rule it out, but it is unlikely to require more expensive confirmatory/diagnostic testing. In other cases, the NNSP will recommend confirmatory/diagnostic testing and consultation or referral with a pediatric sub-specialist when the results are more strongly suggestive of a disorder.

In all cases, whenever a presumptive positive screening result is reported, the NNSP will provide the physician with recommendations for next steps (as approved by the NNSP Advisory Committee), and with contact numbers for available pediatric sub-specialists who can help answer questions.

In cases where quick response time is essential to preventing the damaging effects of the disorder, the newborn's physician is contacted by telephone and provided with information necessary to be able to respond. The NNSP also provides follow-up phone notification after normal business hours, on the weekend and on holidays.

At the October 2005 National Newborn Screening Symposium, two presentations were on communicating results with parents. They noted that many parents have conveyed concern that health care providers should communicate the information with sensitivity. This is especially important at the time of diagnosis. They want to know basic information about the disorder, but don't want to be told they are "lucky" because there is treatment. They do like to know the situation is hopeful, but there is a lot they are trying to absorb. This is a time when they've worried for 9 months about having a health baby, and in most cases believed that they had just that, only to have that dream potentially shattered. Pediatric sub-specialists accustomed to working with patients with these rare disorders can effectively help parents understand their child's disorder and how to manage it while

reassuring them of the positive outcomes that are possible.

Many of the protocols for follow-up can be found at the Nebraska Newborn Screening Program's web-site www.hhss.ne.gov/nsp under the "Physician" link. "ACT" sheets specific to each disorder are available for all disorders required to be screened. CF and CAH information will be posted in January 2006.

Newborn Screening for CYSTIC FIBROSIS

John L. Colombo, MD,
Pulmonologist and Director of
Nebraska's Accredited CF Care Center,
Nebraska Medical Center

The CDC and Cystic Fibrosis Foundation (CFF) have recommended that states begin newborn screening for cystic fibrosis (CF). Several studies have shown benefits of such screening. These include improvements in nutrition, cognitive skills, pulmonary function and reduced medical expenses. In addition, parental anxiety from delayed diagnosis can be lessened. There appears to be a strong likelihood that survival will be improved, although presently there is insufficient long-term data to prove this.

On the other hand, care must be taken to reduce possible negative effects of newborn screening, such as excessive parental anxiety regarding false-positive results and confusion regarding gene carrier status. It is important to communicate quickly and accurately with families having children with positive screens. However, this is not an emergent situation and should not be treated so, as this would provoke unnecessary anxiety. Confirmation should be made with prompt sweat testing in the case of positive screens without a genetic diagnosis (for example, homozygous ΔF508) made by screening. It is recommended by the CFF that this testing be done at an accredited CF Center. If the diagnosis of CF is made, then treatment can be started. The Nebraska CF Center uses a team approach with experienced nutritionists, respiratory therapists, research coordinators and technologists, social workers and nurse specialists, in addition to physicians. Improvement in median life expectancy for CF patients from 12 years to over 35 years during the past four decades is largely attributed to development of such centralized care and research centers.

As with any screening test, there are many “false positives.” Patients with positive screens who turn out to not have CF will outnumber those with CF by approximately 10 to 1. Because of the relatively large number of positive screens relative to positive CF children, it is important to not overly alarm families. Although their wait for confirmation should be short (we will definitely schedule them for sweat testing and evaluation as soon as possible), parents can be reassured somewhat with the knowledge (assuming no family history or symptoms) that their child still only has approximately a 10% chance of having CF. If the child has another disorder known to be associated with elevated IRT, such as perinatal asphyxia, septicemia, hydronephrosis, CMV infection, biliary atresia, trisomy (13, 18, 21), the likelihood of not having CF increases even further. As the confirmatory testing is not emergent, such as it would be for PKU, there is no reason to alarm the family with a weekend or nighttime phone call. Results can usually best be discussed at the two-week office visit.

It is also important to remember that there will be CF cases missed with screening. The false negative rate is generally estimated to be between 2-8%. I believe that for the Nebraska scheme of

screening, we will be towards the lower end of this range. However, this still may mean missing approximately one CF patient every two years. Therefore, it is important to remain vigilant for signs or symptoms of CF, and to not presume that they all would have been detected by screening. It is also very important to remember that children born with intestinal obstruction (meconium ileus or other cause) are likely to yield negative IRT results, and should have CF-DNA studies performed. If these results do not show two CF mutations, a sweat test is indicated when the child reaches 3-4 weeks of age. This is the earliest age at which adequate sweat can commonly be obtained for chloride analysis.

We are very excited about Nebraska becoming one of the early states to institute CF Newborn Screening. We are optimistic that this will further improve outcomes for our patients, by making a diagnosis and instituting treatment before significant complications develop.

If you have any questions, please do not hesitate to contact either the Nebraska Newborn Screening Program office or the Nebraska Regional Cystic Fibrosis Center.

Newborn Screening for CONGENITAL ADRENAL HYPERPLASIA

Richard Lutz, MD, FAAP, FACMG
Pediatric Genetics/Endocrine/Metabolism
Munroe Meyer Institute for Genetics and Rehabilitation, Nebraska Medical Center

The American College of Medical Genetics and the Centers for Disease Control & Prevention have recommended an expanded Newborn Screening panel. Congenital adrenal hyperplasia (CAH) has been recommended for inclusion in the panel because of the potential risk of sudden death and acute illness requiring hospitalization. Because medical intervention is readily available, this has been considered a disease in which newborn screening would offer a benefit. Forty-two States in the USA currently offer screening for CAH. Early pioneers in CAH screening include the states of Alaska and Texas. Because of the deficiency in the adrenal hormones aldosterone and cortisol in severe forms of CAH, the child is at risk for a salt-wasting and adrenal crisis. The adrenal crisis may present toward the end of the first week of life with vomiting, bloating, poor perfusion and hypoglycemia. The salt-wasting crisis usually will be associated with dehydration and weight loss, and the risk of cardiac dysrhythmia, as hyperkalemia develops. The female children may often present with ambiguous genitalia. However, the excessive androgenic hormones will not cause any noticeable difference in the exam of a male infant. Hence, they are often missed. It is thought at this point that classic CAH with salt-wasting crisis occurs in about 1 in 15,000 births in the United States.

All diseases that are screened for in the newborn, including hearing loss, have an association of false positive and false negative results.

As the methods for screening endocrinologic and metabolic disease in the newborn have improved, CAH screening has become more practical. Because the disease is relatively prevalent in our population, it is difficult to identify in the male affected children, and there is potential benefit from presymptomatic treatment, Nebraska has chosen to adopt CAH screening.

17-alpha hydroxy progesterone (17-OHP) will be screened in the initial blood spot, along with the other analytes that are part of the Newborn Screening process. Normal levels for birth weight have been

weight have been developed, and babies whose levels are normal, based on birth weight, will be identified as within normal limits (WNL) or screened normal. Elevations of 17-hydroxy progesterone will lead to a further screening process. Those babies with critical levels will be identified as presumptive positive and their physicians will be contacted. Further extraction steps will help eliminate some false positives. In some cases a repeat blood specimen may be indicated. If the results are inconclusive or presumptive positive, a recommendation for consultation with pediatric endocrinology will be generated. Nebraska's pediatric endocrinologists can advise a primary physician on how to assess the baby, perform diagnostic testing, and the advisability of hospitalization or further medical tests.

Newborn Screening presents the opportunity to prevent deaths from congenital adrenal hyperplasia which still do occasionally occur, especially in the male newborn. It is hoped that babies with classic CAH with salt-wasting will all be identified. Most children with simple virilizing CAH will be identified as well. It's possible that a small number of female children who have relatively normal genitalia may be missed by the Newborn Screening process. However, it's unlikely they will have the salt-wasting form of the disease that could lead to a critical medical problem early in life. The intention of the Program is not to detect children with non-classic CAH, who typically do not have adrenal insufficiency and present later in life with premature adrenarche. The non-classics are at risk for short stature and problems associated with excessive adrenal androgens. Some of these children may be identified in the Newborn Screening process. It is expected that somewhere between two to five children with CAH may be identified annually in the state of Nebraska. The number of false positive tests is unknown at this point, but efforts are being made to minimize that problem. Nebraska's pediatric endocrinologists are excited to help advise primary newborn health providers on how to protect newborn children from the consequences of CAH.

Resources…

CONGENITAL ADRENAL HYPERPLASIA

CARESFoundation
research, education and support for CAH

CARES Foundation, Inc., is committed to education and research for Congenital Adrenal Hyperplasia while providing the resources and the latest information available for managing life with this disorder.

CARES Foundation
189 Main Street
Milburn, NJ 07041
973 912-9395 toll-free 866 277-3737
http://www.caresfoundation.org

Pediatric Endocrinologists in Nebraska:
Munroe-Meyer Institute, Pediatric Endocrinology
Kevin Corley, MD, or Richard Lutz, MD
412 S. Saddle Creek Rd.
Omaha, NE 68131-3707
402 559-9197

Children's Hospital, Pediatric Endocrinology
Monina Cabrera, MD, Jaen Claude Des Mangles, MD
or Adolfo Garnica, MD
8200 Dodge Street
Omaha, NE 68114-4113
402 955-3871

CYSTIC FIBROSIS

National Cystic Fibrosis Foundation
6931 Arlington Road
Bethesda, Maryland 20814
301 955-4422 toll free 800 344-4833
http://www.cff.org/home

Accredited CF Care Centers:
CF Care Center of Nebraska, UNMC
John L. Colombo, MD Director
Emile at 42nd Streets
Omaha, NE 68198-5190
402 559-6275

CF Care Center of Colorado, The Children's Hospital
Frank J. Accurso, MD Director
Denver, Colorado
303 861-6182

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FOR MORE INFORMATION ON NEBRASKA'S NEWBORN SCREENING PROGRAM:

WEB-SITE:	http://www.hhss.ne.gov/nsp
E-MAIL:	newborn.screening@hhss.ne.gov
NNSP Phone:	402 471-9731
NNSP FAX:	402 471-1863

Printing and distribution of this physician's update was made possible by funding from Title V, Maternal and Child Health Block Grant support to the Nebraska Newborn Screening & Genetics Program.

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NEBRASKA HEALTH AND HUMAN SERVICES SYSTEM